09-29-05 07/330446 EOFC

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patentee:	YOSHIMURA ET AL.	Docket:	11613.12USI1
Patent No.:	6,869,924 B1		
Issued:	MARCH 22, 2005		
Title:	HUMAN DERIVED MONOCYTE ATTRACTING PURIFIED PROTEIN PRODUCT USEFUL IN A METHOD OF TREATING INFECTION AND NEOPLASMS IN A HUMAN BODY, AND THE CLONING OF FULL LENGTH CDNA THEREOF		

CERTIFICATE UNDER 37 CFR 1.10:
"Express Mail" mailing label number: EL976595763US
Date of Deposit: September 27 2005

I hereby certify that this paper or fee is being deposited with the U.S. Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to: Certificate of Correction Branch, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

By: _____
Name: David Ortiz

Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

Sir:

We are transmitting herewith the attached:

- ☒ Transmittal Sheet in duplicate containing Certificate of Mailing
- ☒ Request for Certificate of Correction
- ☒ Certificate of Correction
- ☒ Check in the amount of $100.00 for Certificate of Correction for Applicants' Errors
- ☒ Other: Copy of Issue Notification and copy of Amendment filed August 13, 2004 (last filed amendment)
- ☒ Return postcard

Please consider this a PETITION FOR EXTENSION OF TIME for a sufficient number of months to enter these papers, if appropriate. Please charge any additional fees or credit overpayment to Deposit Account No. 13-2725. A duplicate of this sheet is enclosed.

Merchant & Gould P.C.
P.O. Box 2903 Minneapolis, MN 55402-0903
612.332.5300

By: Katherine M. Kowalchyk
Name: Katherine M. Kowalchyk
Reg. No.: 36,848
KKowalchyk:PLSkaw

23552
PATENT TRADEMARK OFFICE

Certificate
SEP 30 2005
of Correction

OCT 5 2005

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent No.:	6,869,924 B1	Docket:	11613.12USI1
Issue Date:	MARCH 22, 2005	Patentee:	YOSHIMURA ET AL.
Title:	HUMAN DERIVED MONOCYTE ATTRACTING PURIFIED PROTEIN PRODUCT USEFUL IN A METHOD OF TREATING INFECTION AND NEOPLASMS IN A HUMAN BODY, AND THE CLONING OF FULL LENGTH CDNA THEREOF		

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By: _____
Name: David Ortiz

REQUEST FOR CERTIFICATE OF CORRECTION

Certificate of Correction Branch
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450

23552
PATENT TRADEMARK OFFICE

Sir:

It is requested that a Certificate of Correction be issued correcting printing errors appearing in the above-identified United States patent. One copy of the text of the Certificate in the suggested form is enclosed.

One of the Patent Office errors listed in the Certificate is to the Patent Term Adjustment. The filing date of the above-identified patent is March 30, 1989. Therefore the patent is not eligible for patent term adjustment. Applicants provide a copy of the Issue Notification which supports Applicants' contention that the application is not eligible for patent term extension. (Exhibit A)

Moreoever, with respect to the correction to the sequence in claim 4 (previously claim 20), Applicants believe this error was due to a Patent Office printing error. Applicants also provide a copy of the last filed amendment showing that the sequence of claim 20 matches that of the corrected sequence. (Exhibit B)

OCT 5 2006

As some of the errors listed are due to Applicants' mistake, our check in the amount of $100.00 is enclosed to cover the Certificate fee.

Issuance of the Certificate of Correction would neither expand nor contract the scope of the claims, and re-examination is not required.

Respectfully submitted,

MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, Minnesota 55402-0903
(612) 332-5300

Date: Sept. 27, 2005

Katherine M. Kowalchyk
Reg. No. 36,848
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EXHIIBIT A

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
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APPLICATION NO.	ISSUE DATE	PATENT NO.	ATTORNEY DOCKET NO.	CONFIRMATION NO.
07/330,446	03/22/2005	[illegible]	1173145P	4539

45074 7590 03/02/2005

NATIONAL INSTITUTES OF HEALTH
P. O. BOX 2903
MINNEAPOLIS, MN 55402

1173.0012USII

ISSUE NOTIFICATION

The projected patent number and issue date are specified above.

Determination of Patent Term Extension or Adjustment under 35 U.S.C. 154 (b)
(application filed prior to June 8, 1995)

This patent application was filed prior to June 8, 1995, thus no Patent Term Extension or Adjustment applies.

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571) 272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at (703) 305-8283.

APPLICANT(S):

TEIZO YOSHIMURA, FREDERICK, MD;
ELIZABETH A. ROBINSON, BETHESDA, MD;
ETTORE APPELLA, CHEVY CHASE, MD;
EDWARD J. LEONARD, CHEVY CHASE, MD;

Verify Patent Term: April 21, 2005
Civil Act/Term: Sept. 18, 2005
Reissue: Mar. 22, 2007

DV SBV

OCT 5 2005

EXHIIBIT B

RESPONSE UNDER 37 C.F.R. 1.116
EXPEDITED PROCEDURE
EXAMINING GROUP

S/N 07/330,446

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	Yoshimura, et al.	Examiner:	Carlson, Karen C.
Serial No.:	07/330,446	Group Art Unit:	1653
Filed:	March 30, 1989	Docket No.:	11613.0012USI1
Confirmation No.:	4539	Customer No.:	23552
Title:	HUMAN DERIVED MONOCYTE ATTRACTING PURIFIED PROTEIN PRODUCT USEFUL IN A METHOD OF TREATING INFECTION AND NEOPLASMS IN A HUMAN BODY, AND THE CLONING OF FULL LENGTH CDNA THEREOF		

CERTIFICATE UNDER 37 CFR 1.6(d):
I hereby certify that this paper is being transmitted by facsimile to the U.S. Patent and Trademark Office on August 13, 2004.

By: Sheryl A. Boerboom
Name: Sheryl A. Boerboom

AMENDMENT UNDER 37 C.F.R. § 1.116

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

This is a response to the outstanding Office Action mailed on March 8, 2004.

Amendments to the Claims are reflected in the listing of claims that begins on page 2 of this paper.

Remarks begin on page 9 of this paper.

Amendments to the Claims:

This listing of claims will replace all prior versions and listings of claims in the application:

Listing of Claims

1. (Previously Amended) A pure peptide product derived from human glioma cells exhibiting monocyte chemotactic activity at a concentration of 1 nM; said peptide product exhibiting an estimated molecular mass of about 8,400 daltons.

2. (Currently Amended) The pure peptide product of claim 1 obtained by the process comprising the steps of:

(I) culturing live cells derived from:

(a) human glioma cell line U-105MG, or

(b) human peripheral blood mononuclear leukocytes, in an appropriate growth medium

(II) separating said cells from said growth medium;

(III) chromatographing said growth medium on an Orange-A Sepharose column, utilizing an appropriate solvent, and collecting the fractions which contain the desired peptides;

(IV) chromatographing said peptide containing fraction obtained in Step III on an appropriate cation-exchange HPLC column, utilizing appropriate solvents, and collecting the fractions which contain said desired peptides;

(V) chromatographing said peptide containing fractions obtained in Step IV on a reverse phase HPLC column, utilizing an appropriate solvent, and collecting the fractions containing said desired peptides; and

(VI) removing liquid from said peptide containing fractions obtained in Step V, to give said peptide product ~~as~~ in a solid form.

3. (Previously Amended) The pure peptide product of claim 1, which is derived from glioma cell line U-105MG, said peptide product comprising an amino acid

sequence of:

1 10 20 30
XPDAINAPVTCCYNFTNRKISVQRLASYRRITSSKCPKE

40 50 60 70
AVIFKTIVAKEICADPKQKWVQDSMDHLDKQTQTPKT

wherein:

A is Alanine;
C is Cysteine;
D is Aspartic Acid;
E is Glutamic Acid;
F is Phenylalanine;
H is Histidine;
I is Isoleucine;
K is Lysine;
L is Leucine;
M is Methionine;
N is Asparagine;
P is Proline;
Q is Glutamine;
R is Arginine;
S is Serine;
T is Threonine;
V is Valine;
W is Tryptophan;
Y is Tyrosine; and
X is pyroglutamic acid.

4. (original) A method of preparing a pure peptide product, having a molecular weight of about 8,400 daltons, and exhibiting optimal monocyte chemotactic activity at a concentration of 1 nM ; said method comprising the steps of:

(I) culturing live cells derived from:

(a) human glioma cell line U-105MG, or

(b) human peripheral blood mononuclear leukocytes, in an appropriate growth medium;

(II) separating said cells from said growth medium;

(III) chromatographing said growth medium on an Orange-A Sepharose column, utilizing an appropriate solvent, and collecting the fractions which contain the desired peptides;

(IV) chromatographing said peptide containing fractions obtained in Step III on an appropriate cation-exchange HPLC column, utilizing appropriate solvents, and collecting the fractions which contain said desired peptides;

(V) chromatographing said peptide containing fraction obtained in Step IV on a reverse phase HPLC column, utilizing an appropriate solvent, and collecting the fractions containing said desired peptides; and

(VI) removing liquids from said peptide containing fractions obtained in Step V, to give said peptide product in a solid form.

5. (Cancelled)

6. (Original) A method of treating neoplasms in a human which comprises administering to a human an effective neoplasm treating amount of the purified peptide product of claim 1.

7. (Original) A pharmaceutical composition comprising:
the pure peptide product of claim 1; and
a pharmaceutically acceptable carrier therefor.

8-19. (Cancelled)

20. (Currently Amended) A pure peptide ~~produce~~ product exhibiting optimal monocyte chemotactic activity at a concentration of 1 nM, said peptide product exhibiting an estimated molecular mass of about 8,400 daltons and comprising an amino acid sequence of:

1 10 20 30
XPDAINAPVTCCYNFTNRKISVQRLASYRRITSSKCPKE

40 50 60 70
AVIFKTIVAKEICADPKQKWVQDSMDHLDKQTQTPKT

wherein:

A is Alanine;
C is Cysteine;
D is Aspartic Acid;
E is Glutamic Acid;
F is Phenylalanine;
H is Histidine;
I is Isoleucine;
K is Lysine;
L is Leucine;
M is Methionine;
N is Asparagine;
P is Proline;
Q is Glutamine;
R is Arginine
S is Serine;
T is Threonine;
V is Valine;
W is Tryptophan;
Y is Tyrosine; and
X is pyroglutamic acid;

or ~~a substantially homologous amino acid sequence thereto~~ conservative amino acid substitutions thereof.

21-25. (Cancelled)

26. (New) A recombinant peptide comprising the amino acid sequence:

1 10 20 30
QPDAINAPVTCCYNFTNRKISVQRLASYRRITSSKCPKE

40 50 60 70
AVIFKTIVAKEICADPKQKWVQDSMDHLDKQTQTPKT

wherein:

A is Alanine;
C is Cysteine;
D is Aspartic Acid;
E is Glutamic Acid;
F is Phenylalanine;
H is Histidine;
I is Isoleucine;
K is Lysine;
L is Leucine;
M is Methionine;
N is Asparagine;
P is Proline;
Q is Glutamine;
R is Arginine
S is Serine;
T is Threonine;
V is Valine;
W is Tryptophan; and
Y is Tyrosine;

or conservative amino acid substitutions thereof.

27. (New) An isolated peptide comprising an amino acid sequence encoded by a nucleic acid sequence having a sequence of:

CAG CCA GAT GCA ATC AAT GCC CCA GTC ACC TGC TGT TAT AAC TTC ACC AAT AGG AAG ATC TCA GTG CAG AGG CTC GCG AGC TAT AGA AGA ATC ACC AGC AGC AAG TGT CCC AAA GAA GCT GTG ATC TTC AAG ACC ATT GTG GCC AAG GAG ATC TGT GCT GAC CCC AAG CAG AAG TGG GTT

CAG GAT TCC ATG GAC CAC CTG GAC AAG CAA ACC CAA ACT CCG AAG ACT

28. (New) An isolated peptide obtained by a process comprising the steps of:

(I) culturing a host cell transformed with a nucleic acid encoding a polypeptide comprising the amino acid sequence:

1 10 20 30
QPDAINAPVTCCYNFTNRKISVQRLASYRRITSSKCPKE

40 50 60 70
AVIFKTIVAKEICADPKQKWVQDSMDHLDKQTQTPKT

wherein:

A is Alanine;
C is Cysteine;
D is Aspartic Acid;
E is Glutamic Acid;
F is Phenylalanine;
H is Histidine;
I is Isoleucine;
K is Lysine;
L is Leucine;
M is Methionine;
N is Asparagine;
P is Proline;
Q is Glutamine;
R is Arginine
S is Serine;
T is Threonine;
V is Valine;
W is Tryptophan; and
Y is Tyrosine;

or conservative amino acid substitutions thereof.

(II) recovering the polypeptide from the cell.

29. (New) A method of treating neoplasms in a human which comprises administering to a human an effective amount of the peptide of any of claims 26-28.

30. (New) A pharmaceutical composition comprising:
the peptide of any of claims 26-28; and
a pharmaceutically acceptable carrier therefor.

REMARKS

Applicant has carefully reviewed and considered the Office Action mailed on March 8, 2004, and requests reconsideration of the rejection of the claims.

Claims 21 - 25 are cancelled without prejudice or disclaimer. Applicants reserve the right to pursue the subject matter of these claims in one or more continuation applications.

Claims 2 and 20 have been amended. Claim 2 was amended to delete the typographic error "as" in the last line of the claim. Claim 20 was amended to correct a typographic error and to clarify the claim. The amendment to claim 20 is supported throughout the specification, including at page 11, lines 1-6.

Claims 26 - 30 have been added. Support for the added claims can be found in throughout the specification including at page 4 line 9 to page 5 line 21; page 14, lines 1-16; page 16, line 12 to page 17, line 21; and page 42, line 19 to page 43, line 8. No new matter has been added.

Accordingly, claims 1-4, 6, 7, 20, and 26 -30 are pending in this application.

Applicants thank the Examiner for properly re-setting the mailing date of the present office action from January 8, 2004 to March 8, 2004.

Interview

Applicants thank Examiner Carlson for the interview conducted on August 12, 2004. Applicants discussed cancelling claims 21-25 and presenting new claims 26-30. Applicants discussed that the sequence of claims 26 and 28 have a glutamine at the N terminus rather than pyroglutamic acid and that this sequence is described in the specification. We also discussed language regarding conservative amino acid substitutions.

Applicants also submit herewith Gong et al, J. Exp. Med., 181:631 (1995) as Exhibit A and Van Coillie et al., Biochemistry, 37:12672 (1998) as Exhibit B. The Gong et al. reference (Exhibit A) clearly indicates that a wild type pyroglutamic is not essential for binding and function of MCP-1. (See page 634). The Van Coillie et al. reference

shows that there is heterogeneity regarding MCP proteins in that the pyroglutamic of MCP-2 is required for chemotactic activity. (See page 12678, column 2). The authors also note that the pyroglutamic acid is not essential for activity of MCP-1. (See page 12678, column 2).

35 U.S.C. §112, first paragraph

Claims 21-25 were again rejected under 35 U.S.C. §112, first paragraph, as lacking a written description for non-human sources of the protein. The examiner's position remains essentially unchanged from the prior office action mailed February 15, 2000. Applicants maintain their traverse to the rejection for the reasons stated in the amendment filed August 15, 2000. However, in order to expedite prosecution and permit the remaining claims, indicated allowable, to proceed to issue Applicants' have cancelled claims 21-25 and reserve the right to pursue them in a separately filed continuation application.

Obviousness-type Double Patenting

Claims 1-4, and 6-7 were rejected under obviousness-type double patenting. These claims resulted from a restriction requirement of June 22, 1989 of then copending application USSN 07/304,234, now abandoned, refiled as USSN 07/686,264, now U. S. Patent 6,090,795. A Terminal Disclaimer of the present claims over claims 18-29 of co-pending USSN 07/686,264, now U.S. Patent 6,090,795, is enclosed to overcome the obviousness-type double patenting rejection of all pending claims.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. If the Examiner believes a telephone conference would advance the prosecution of this application, the Examiner is invited to telephone the undersigned at (612) 336-4686 or the below-listed main telephone number.

Respectfully submitted,

MERCHANT & GOULD P.C.
P.O. Box 2903
Minneapolis, MN 55402-0903
(612) 332-5300

Date: August 13, 2004

Katherine M. Kowalchyk
Katherine M. Kowalchyk
Reg. No. 36,848

23552
PATENT TRADEMARK OFFICE

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,869,924 B1 **PAGE** 1 **of** 2

DATED : MARCH 22, 2005

INVENTOR(S) : YOSHIMURA ET AL.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Front page, (*) Notice, line 3: "by 1,826 days." should read --by 0 days.--

Col. 1, line 18: "thought in include" should read --thought to include--

Col. 2, line 32: "X is pyrolutamic acid." should read --X is pyroglutamic acid.--

Col. 4, line 33: ""The term "LAMBDA" should read --The term "LAMBDA--

Col. 4, line 40: "Calif. 92037."" should read --Calif. 92037.--

Col. 4, line 47: "and extend of determined" should read --and extent of determined--

Col. 8, line 30: "include the B-lactamase" should read --include the β-lactamase"

Col. 9, line 17: "linear Nacl gradients" should read --linear NaCl gradients--

Col. 14, lines 31-32: "Line U-150MG Derived" should read --Line U-105MG Derived--

Col. 17, line 50: "Lambda ZAP II vector" should read --Lambda ZAP II® vector--

Col. 18, line 2: "Approximately 5x10" should read --Approximately $5x10^5$--

Col. 18, line 34: "cytokines: IL-Lβ, IL-2," should read --cytokines: IL-1β, IL-2,--

Col. 18, line 62: "LAMBDA ZAP II." should read --LAMBDA ZAP II®.--

Col. 24, line 27: "X is tryosine; and" should read --Y is tyrosine; and--

Col. 24, line 28: "Y is pyroglutamic acid." should read --X is pyroglutamic acid.--

MAILING ADDRESS OF SENDER:
Merchant & Gould P.C.
Attn: Katherine M. Kowalchyk
P.O. Box 2903
Minneapolis, MN 55402-0903

PATENT NO. 6,869,924 B1

Docket No. 11613.12USI1

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OCT 5 2005

FORM 1050

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,869,924 B1 **PAGE** 2 **of** 2

DATED : MARCH 22, 2005

INVENTOR(S) : YOSHIMURA ET AL.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

Col. 27, line 23, claim 2: "obtained in Step IV" should read --obtained in Step III--

Col. 27, line 28, claim 2: "obtained in Step 1V" should read --obtained in Step IV--

Col. 27, line 34, claim 2: "peptide product as" should read --peptide product--

Col. 28, line 6, claim 4: "AVLFKTTYAKEICADPKQKWVQDSMDHLDKRTQTPKT" should read --AVIFKTIVAKEICADPKQKWVQDSMDHLDKRTQTPKT--

Col. 28, line 24, claim 4: delete duplicate "or conservative amino acid substitutions thereof."

Col. 28, line 53, claim 6: "an no acid sequence" should read --an amino acid sequence--

Col. 30, line 15, claim 10: "appropriate cation change" should read --appropriate cation-exchange--

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Minneapolis, MN 55402-0903

PATENT NO. 6,869,924 B1

Docket No. 11613.12USI1

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